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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/977,155	10/12/2001	Joachim Herz	UTSD:0862	3854

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EXAMINER

COOK, LISA V

ART UNIT	PAPER NUMBER
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1641

DATE MAILED: 12/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/977,155

Applicant(s)

HERZ ET AL.

Examiner

Lisa V. Cook

Art Unit

1641

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 23 December 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-20 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4-4/2/04. 6) ☐ Other:

## **DETAILED ACTION**

### ***Response to Notice to Comply***

1. Applicants' response to the Notice dated 09 December 2002 (Paper #3 filed 12/23/02) is acknowledged. In response to the notice applicant contends that all the cited amino acid references are directed to portions of a known DNA. This argument was found persuasive. Accordingly the Notice to Comply is vacated.

2. Currently claims 1-20 are pending and under consideration.

### ***Priority***

3. No priority claim to an application in which the benefits of an earlier filing date is desired in the instant application.

### ***Drawings***

4. No drawings were filed in this application.

### ***Information Disclosure Statement***

5. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the examiner on form PTO-892 or applicant on form PTO-1449 cited the references they have not been considered. See the disclosure, page 1 lines 30-32 for example.

6. The Information Disclosure Statement filed 03 January 2003 has been considered on the merits prior to first action.

Art Unit: 1641

7. The Information Disclosure Statement filed 02 April 2004 has been considered on the merits prior to first action. However, the IDS filed April 2, 2004 appears to be directed to another application because the material contained therein is not applicable to the instant invention. Although the application number listed 09/977,155; the filing date, inventor, art unit, and attorney docket number were incorrect.

### ***Claim Objections***

8. Claims 1, 8, and 11-20 are objected to because of the following informalities: Claims 1, 8 and 11-20 utilize acronyms (see LDL, LRP, LRP1b, LDLR, VLDLR, ApoER2, MEGF7, LRP5, LRP6 and LR11). Although the terms may have art-recognized meanings, it is not clear if applicant intends to claim any prior art definition of the abbreviations. The terms should be defined in their first instance. The initial explanation will convey intended meaning of subsequent abbreviations in the claims. Please define.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

9. Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 1 is vague and confusing. The preamble of the claim reads on "detecting the proteolysis of an LDL receptor". However the body of claim is directed to the detection of a released tail.

Art Unit: 1641

Therefore the method claims do not clearly complete the intended outcome set forth in the preamble. It is suggested that the claims include the detection of the proteolysis product of the LDL receptor for clarity. Appropriate correction is required.

B. In claims 9 and 12-20 it is not clear how the protease will be native to the membrane. If the protease is apart of the membrane, it is not clear as to how cleavage into a C-terminal tail will occur. Does applicant intend to mean a "protease cleavage site" will be native to the membrane, such that cleavage will occur in the presence of a protease? Clarification is required.

*Note: In order to promote compact prosecution claims 9 and 12-20 have been interpreted to read on a "protease cleavage site" native to the membrane.*

***Claim Rejections - 35 USC § 102***

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

I. Claims 1-9 and 11-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Willnow et al. (The Journal of Biological Chemistry, Vol.269, No.22,15827-15832, 1994).

Art Unit: 1641

Willnow et al. teach methods involving LRP-mini receptors. See abstract. The LRP-mini receptor comprises 11 complement-type repeats (LDL receptor ligand – polypeptide) and one EGF precursor homologous domain (region IV) is fused to the carboxyl-terminal segment of LRP (six EGF repeats, transmembrane segment, and the cytoplasmic tail). See page 5828, 2<sup>nd</sup> column, 1<sup>st</sup> paragraph, and figure 1. Region IV contains a proteolytic site, which allows for protease digestion into a 80kDa amino-terminal and a 85kDa carboxyl-terminal fragment (C-terminal tail).

The LRP regions were prepared via SDS gel electrophoresis and transferred to nitrocellulose (solid-phase affinity adsorption). Polyclonal anti-LRP antibodies directed against the cytoplasmic tail of LRP and <sup>125</sup>I goat anti-rabbit IgG (affinity tag) were utilized in Western blotting procedures to detect the mini receptors membrane extracts from the cell lines. Bottom of page 15828 to 15829 and figure 2.

II. Claims 1-3, 5, and 7-14 are rejected under 35 U.S.C. 102(a) as being anticipated by Kinoshita et al. (The Journal of Neuroscience, 11/1/01, 21(2) 8354-8361).

Kinoshita et al. teach a protein construct involving APP and LRP interaction. The extracellular domains of LRP and APP bind by ligand-ligand interaction (polypeptide fused to a C-terminal). In this way LRP serves as a internalization receptor for APP. The APP is cleaved by  $\alpha$  or  $\beta$  secretases to release soluble APP and membrane bound C-terminal fragments. An additional cleavage in the transmembrane domain by  $\gamma$ -secretase results in 4 kDa amyloid- $\beta$  peptides. See page 2 of 20. The c terminus in both APP and LRP are tagged and identified with antibodies. See figure 1 and page 5 of 20, 2<sup>nd</sup> and 3<sup>rd</sup> paragraphs.

Art Unit: 1641

***Claim Rejections - 35 USC § 103***

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

III. Claims 15-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Willnow et al. (The Journal of Biological Chemistry, Vol.269, No.22,15827-15832, 1994) or Kinoshita et al. (The Journal of Neuroscience, 11/1/01, 21(2) 8354-8361) in view of Herz (Neuron, Vol29, pages 571-581).

Please see Willnow et al. and Kinoshita et al. as set forth above.

Art Unit: 1641

Willnow et al. and Kinoshita et al. differ from the instant invention in not teaching all the possible LDL receptor (namely LRP, LRP1b, megalin, LDLR, VLDLR, ApoER2, MEGF7, LRP5, LRP6, and LR11).

However, Herz discloses the core members of the LDL receptor gene. See abstract and figure 1. Herz further teaches each LDL possible role and involvement in cellular events. See Table 1. The core members of the LDL receptor gene family include the LDL receptor, LRP, megalin, VLDL, ApoER2, LrP1b, and MEGF7. See page 571, 1<sup>st</sup> column, 2<sup>nd</sup> paragraph. Herz et al. disclose that these seven core members of the LDL receptor gene family are “structurally closely related cell surface receptor”.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use various known LDL receptor equivalents having similar structures and found native to the membrane as taught by Herz in the method of Willnow et al. and Kinoshita et al. because Herz taught that the LDL receptor gene family consists of seven structurally related cell surface receptors (LDL receptor, LRP, megalin, VLDL, ApoER2, LrP1b, and MEGF7). See abstract. Therefore the analysis of any of the known equivalent receptors taught by Herz in the method of Willnow et al. and Kinoshita et al. would have been obvious because the receptors would perform the same function in the same manner as the receptors found in Willnow et al. and Kinoshita et al. In other words the behavior of one compound predicts the behavior of equivalents absent evidence to the contrary. Further, applicant has not set forth reasons for the utility of any particular receptor. Accordingly, obviousness is based on the similarity of structure, function, and similar properties. In re Payne, 606 F.2d 303, 203, USPQ 245, 254-55 (CCPA 1979).



Art Unit: 1641

***Remarks***

11. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

A. Tan et al. (Biochimica et Biophysica Acta, 7/1/98, Vol1407, No1, pages 69-78)

Abstract Only - disclose constructs including an LDL receptor.

12. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 Fax number is (703) 872-9306, which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (571) 272-0823.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.


Art Unit: 1641

Status information for unpublished applications is available through Private PAIR only.


For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should

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Business Center (EBC) at 866-217-9197 (toll-free).



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